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Measuring Somatic Symptoms With the CES–D to Assess Depression in Cancer Patients After Treatment: Comparison Among Patients With Oral/Oropharyngeal, Gynecological, Colorectal, and Breast Cancer

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There is a high prevalence of depression after cancer treatment. In the literature, several authors have raised questions about assessing somatic symptoms to explore depression after cancer treatment. These somatic sequelae are a consequence of cancer treatment and should cause higher depression rates in cancer patients. In this study, the Somatic domain on a depression questionnaire, the Center for Epidemiologic Studies–Depression scale (CES–D) was analyzed in different cancer patients after treatment, as compared with a control group. Data from 566 cancer patients (oral/oropharyngeal, gynecological, colorectal, and breast cancer) and 255 randomly chosen comparison patients were analyzed. The total score on the CES–D domain of Somatic Retarded Activity significantly differed between the cancer and comparison groups; but the cancer groups showed both less somatic morbidity (colorectal cancer) and more somatic morbidity (oral/oropharyngeal, breast) than the comparison group. In the analyses of the CES–D with and without the Somatic domain, the prevalence of depression symptoms with the Somatic domain is lower for the cancer groups. Authors conclude that cancer patients are not a homogenous group as regards somatic sequelae. Evidence for removing Somatic items from the CES–D for patients after cancer treatment was not confirmed. (Psychosomatics 2006; 47:465–470)

Survival rates of several cancer types have increased because of earlier detection and better treatment approaches.[1] As a consequence, more patients have to cope with the physical and emotional consequences of the diagnosis of cancer and the side effects of treatment. In the last decade, more attention has been given to this group of patients. Important in posttreatment cancer research are quality of life,[2] coping,[3,4] depression,[5,6] somatic morbidity,[7,8] pain,[9–11] and fatigue.[12,13] This research has led to a better understanding of physical and emotional problems after cancer treatment, and, as a consequence, treatment programs have been developed, such as: post-cancer treatment rehabilitation programs,[14] psychosocial interventions,[15,16] pain management,[10] and multidisciplinary programs.[17]

A major important outcome after cancer treatment is depression. The prevalence of depression after cancer treatment is about 24% (range: 1.5% to 50%).[18] Depression

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affects quality of life, survival, length of hospital stay, and therapy compliance.[5,18,19] It is therefore clinically important to recognize depression in the posttreatment phase of cancer patients. Physicians are often not well trained in recognizing depression;[20] therefore, a questionnaire is helpful for exploring depression symptoms during the medical follow-up.

According to DSM-IV, a depressive episode is assumed if five (or more) out of nine symptoms (see Appendix 1) are present; also, the symptoms should be present during the same 2-week period and represent a change from previous functioning.[21] Symptoms of a clinical depression in patients after cancer treatment can be assessed through a clinical interview, a (semi)-standardized interview, or a questionnaire. Questionnaires are most frequently used in the medical setting and for clinical cancer research.

The prevalence of depression in cancer patients is related to type of cancer, follow-up, medical illness, gender, and method of assessment.[18,19,22,23] Several authors have also suggested that the high prevalence of depression after cancer treatment is due to the fact that the somatic symptoms of depression are similar to the somatic symptoms caused by the cancer treatment, itself.[6,22,24,25] They state that somatic symptoms should not be measured when assessing depression in cancer patients. Some authors have even removed somatic items from depression questionnaires,[24,25] and, in the Hospital Anxiety and Depression Scale (HADS), somatic symptoms are not even included in the depression scale.[26]

Hard evidence for the hypothesis that somatic symptoms should be removed in a depression questionnaire when assessing cancer patients is virtually missing, although some studies have been performed to explore this hypothesis. In one study exploring the role of somatic items in cancer patients, the Zung Self-Rating scale was divided into a questionnaire with and without somatic items. The outcome on the questionnaire with somatic items was about 5% higher. The authors stated that the Zung Self-Rating scale has 5% more false-positive depressed cancer patients when somatic items are included.[24] After a factor analyses of the Zung Self-Rating depression scale, Passik et al.[27] found that fatigue is the only somatic item that is typically a symptom of depression in cancer patients; this is in contrast with the results of Visser and Smets,[25] who found no relationship between depression and fatigue. They stated that fatigue is not a valid criterion for depression for patients after radiation therapy. After analyzing a structured interview with cancer patients Akechi et al.[28] found that eating disorders and concentration problems were strongly related to depression, whereas sleep disorders and fatigue were related to the somatic sequelae of cancer treatment.[28] During radiotherapy in oral and oropharyngeal cancer patients, several eating-related side effects are described, which affect the outcome of depression questionnaires.[29,30] From these studies, no clear conclusion can be made about the role of somatic items in the assessment of depression in cancer patients.

From the above, it is clear that the prevalence of depression in cancer patients is high, and there is concern about a potential similarity of the somatic symptoms caused by cancer treatment and those caused by depression; these similarities may increase the percentages of false-positive depression findings assessed with a questionnaire when somatic items are included. The aim of this study was to analyze the influence of somatic symptoms on the CES–D in cancer patients after treatment, as compared with a control group, and to analyze this influence between cancer types.

METHOD

The CES–D is a short self-report scale designed to measure depressive symptoms.[31] The questionnaire was translated into Dutch; it contains 20 items, divided in four domains: Somatic Retarded Activity (7 items), Depressed Affect (5 items), Positive Affect (4 items), and Interpersonal Affect (2 items), and 2 single items that complete the total score.[32,33] The total score ranges from 0 to 60; a score of ≥ 16 indicates a depressed symptomatology. The CES–D is often administered to inpatients with cancer. The CES–D in cancer patients has a good internal consistency ($\alpha = 0.89$) and the test–retest reliability was 0.51 ($p < 0.001$). The construct validity and internal consistency of the CES–D are good.[32] The positive predictive value is 54.5% for the cut-off score of 16 in head and neck cancer patients.[34] The CES–D is appropriate for use in clinical psychosocial research.[35]

In the current study, the CES–D was administered to patients at least 1 year after the first cancer treatment (and to a control group). Patients with tumor recurrences were excluded.

The data of comparison subjects and patients with breast, colorectal, and gynecological cancer were obtained from the database of the Northern Centre for Health Care Research (NCG).[36] The comparison group was matched for gender and age with the cancer group and lived in the same area as the patients with cancer. Patients with oral/oropha-

ryngeal cancer were assessed in the University Hospital, Groningen, in the Department of Oral and Maxillofacial Surgery; the Department of Otorhinolaryngology, Head, and Neck Surgery; or the Department of Surgical Oncology. The CES–D was assessed during a regular appointment in the outpatient clinic. Patients received a letter 1 week before their appointment, in which the study was explained. Their medical doctor asked the patients to participate. If patients were willing to participate, an informed-consent was signed, and the CES–D was filled out. The Review Board of the hospital approved the study.

Statistical Analysis

For the statistical analysis, we used SPSS 10.0. We tabulated descriptive data (gender, age, treatment, depression symptoms); relative risk (RR) and 95% confidence intervals (CI) were calculated with the CIA (Confidence Interval Analyses, 2nd Version). The CES–D total scores, Somatic Retarded Activity scores, and the Depressed Affect scores were also calculated. The comparison and the cancer groups were compared on the CES–D total, and the domains of Somatic Retarded Activity and Depressed Affect were compared by ANOVA. Also, a multi-comparison was performed among the control group and four cancer groups on the CES–D total, and the domains of Somatic Retarded Activity and Depressed Affect, with a Bonferroni post-hoc correction. We performed a Kruskal-Wallis test as control for the outcome on the ANOVA multi-comparison tests because the outcomes on the CES–D were not normally distributed.

Correlations (Spearman ρ) between the domains of Somatic Retarded Activity and Depressed Affect were analyzed for the comparison group and cancer patients. A new cut-off point for depressed symptoms was calculated for the CES–D without the Somatic items, as previously described with the Zung depression scale.[24] If a patient had a score of ≥ 16, in the 20-item version, there is an indication of depression symptoms (16/20, or 0.8). Therefore the new cut-off point for the 13-item version is 10 (0.8×13 [without Somatic items]) $= 10.4$).

We used the McNemar test to compare the CES–D with and without the Somatic items.

RESULTS

In this cross-sectional study with reference-group data, we analyzed data from 509 patients and 223 randomly chosen comparison subjects. Descriptive data are presented in Table 1. The breast and gynecological cancer patients were typically women. Patients with depression symptoms, according to the CES–D, are listed in Table 1. The prevalence of depression symptoms in the cancer groups was 16% (oral/oropharyngeal), 22% (breast cancer), and 23% (gynecological group); this is a bit lower than reported in the literature, and the prevalence for colorectal cancer was surprisingly low, at 7%. In Table 2, the results of the ANOVA between groups are presented. The cancer group scored significantly higher than the control group on the domain of Somatic Retarded Activity and Depressed Affect. The four cancer groups and the comparison group differ significantly on Total score, Somatic Retarded Activity, and Depressed Affect scores (Table 2). In the ranking of the Kruskal-Wallis (not presented in the table) the colorectal patients scored the lowest on all scales. Oral/oropharyngeal patients and breast cancer patients scored highest for Somatic Retarded Activity. The Total score, the Somatic Retarded Activity score and Depressed Affect score were significantly ($p < 0.01$) different for the cancer groups and comparison group. The outcomes on the Kruskal-Wallis test were similar to the outcome on the ANOVA multi-comparison analysis. The correlations between the domains of Somatic Retarded Activity and Depressed Affect were significant for the control group (0.54; $p < 0.01$) and the cancer group (0.66; $p < 0.01$).

The CES–D with and without depression symptoms and with and without the somatic items are presented in Table 3. The cancer groups, except the oral/oropharyngeal patients, and comparison group showed significantly higher incidences of depression symptoms without the Somatic items, as compared with the CES–D with Somatic items.

DISCUSSION

Cancer patients are not a homogeneous group with respect to the outcome of the CES–D and the domains of Somatic Retarded Activity and Depressed Affect. As compared with a control group, cancer patients score lower (colorectal) as well as higher (breast, oral/oropharyngeal) on the domain of Somatic Retarded Activity. Somatic sequelae for each type of cancer differ, and, therefore, "the cancer patient" does not exist. After removing the Somatic items of the CES–D to assess depression in cancer patients, the percentages of patients with depression symptoms increases. The hypothesis that the prevalence of false-positive depression increases when Somatic items are included in the CES–D could not be verified in the current study. The cor-

TABLE 1. Descriptive Data (Gender, Age) of the Control Group, Cancer Patients, and Cancer Subgroups, Type of Treatment, and Number of Patients With Depression Symptoms, According to the CES–D

	Control Group	Cancer (All Subgroups)	Breast Cancer	Colorectal Cancer	Gynecological Cancer	Oral and Oropharyngeal Cancer
N	223	509	189	104	62	154
Female gender	70% (155)	67% (340)	99% (188)	38% (40)	100% (62)	33% (50)
Age, years, mean (SD)	57 (15)	59 (14)	55 (13)	65 (12)	54 (16)	61 (12)
Surgery	—	99% (504)	98% (186)	100% (104)	97% (60)	100% (154)
Radiation therapy	—	48% (245)	54% (102)	11% (11)	42% (26)	69% (106)
Chemotherapy	—	19% (99)	42% (80)	7% (7)	19% (12)	0% (0)
Depressive symptomatology[a]	10% (23)	17% (87)	22% (41)	7% (7)	23% (14)	16% (25)
Relative risk [b] (95% CI)	1.00	1.66 (1.08–2.55)	2.10 (1.31–3.37)	0.65 (0.29–1.47)	2.19 (1.20–3.00)	1.57 (0.91–2.67)

Values are percent (N), unless otherwise noted. Relative risks, 95% confidence intervals of depressed symptomatology, are presented for the cancer patients and the cancer subgroups. CI: confidence interval.

[a]CES–D score ≥16.

[b]The control group is the reference group.

CES–D: Center for Epidemiological Studies–Depression scale.

TABLE 2. Scores on the CES–D Total, the Domains of Somatic Retarded Activity (7 items), and Depressed Affect (5 items)

	CES–D Total	p	Somatic Retarded	p	Depressed Affect	p
Cancer group total	9.0 (8.5)	0.26	3.0 (3.4)	0.006	1.6 (2.5)	<0.001
Control group (C)	8.3 (6.4)		2.3 (2.6)		0.9 (1.7)	
Breast (B)	10.5 (8.3)		3.3 (3.2)		1.9 (2.6)	
Colorectal (CR)	7.0 (6.7)		1.7 (2.4)		0.9 (1.8)	
Gynecological (G)	9.4 (9.6)		2.6 (3.5)		1.9 (3.0)	
Oral and oropharyngeal (O)	8.3 (8.9)	0.002	3.8 (4.0)	<0.001	1.5 (2.4)	<0.001

Presented are the ANOVA for comparisons between groups (control versus cancer) and an ANOVA with multiple comparison (with Bonferroni correction) between the control and four cancer subgroups.In the multiple corrected comparisons, significant differences ($p<0.05$) were found for the following domains: CES–D Total: C–B, B–CR; Somatic Retarded: C–B, C–O, B–CR, CR–O; and Depressed Affect: C–B, C–G, B–CR, CR–G.

CES–D: Center for Epidemiological Studies–Depression scale.

TABLE 3. Number of Patients With and Without Depression Symptomatology, as Measured With the CES–D, With and Without the Somatic Domain

	Depression Symptomatology, With Somatic Domain	Depression Symptomatology, Without Somatic Domain		p
		No	Yes	
Control N = 223	No	172 (77%)	23 (10%)	<0.001
	Yes	0 (0%)	28 (13%)	
Breast N = 189	No	125 (66%)	21(11%)	<0.001
	Yes	4 (2%)	39 (21%)	
Colorectal N = 104	No	87 (84%)	10 (10%)	0.012
	Yes	1 (1%)	6 (6%)	
Gynecological N = 62	No	42 (68%)	6 (10%)	0.031
	Yes	0 (0%)	14 (23%)	
Oral and oropharyngeal N = 154	No	124 (81%)	5 (3%)	0.453
	Yes	2 (1%)	23 (15%)	

A McNemar test was performed to analyze the influence of the Somatic items on the CES–D for the four cancer groups and control group. Percentages are cell percentages.

CES–D: Center for Epidemiological Studies–Depression scale.

relation between Somatic items and the Depressed Affect items is considerable, indicating that the domains were interrelated and, as in the construct of depression, cannot be separated.

The influence of gender on outcome of depression questionnaires is known to be significant.[37] The patients with breast and gynecological cancer were predominantly women, and the percentages of patients with depression symptoms and the scores on the domain of Depressed Affect are the highest in these two cancer groups. Whether these high scores are the effect of cancer type, female gender, or both cannot be distinguished in this study. In contrast, oral/oropharyngeal patients score significantly higher on the Somatic Retarded Activity domain. Oral/oropharyngeal cancer surgery is often extensive surgery, leading to considerable morbidity, often followed by radiation therapy, which may explain the high scores on the Somatic Retarded Activity scale. Patients after colorectal cancer therapy score lower on all outcomes; the number of female patients in this group is low, and the number of patients with double treatment, for instance, surgery and radiation therapy, is also lower. Receiving two treatment modalities might affect the prevalence of depression, and this might be an interesting topic for further studies.

In the current study, somatic morbidity does not increase the prevalence of depression symptoms as measured with the CES–D; on the contrary—depression symptoms were more frequently present without the Somatic items. This is in contrast with the study of Dugan et al.,[24] who analyzed the Zung Self-Rating depression scale with and without somatic items, reporting 5% more false-positives when measuring depression symptoms with somatic items.

It would be valuable in further studies to compare several depression questionnaires on the influence of the somatic items because it seems that the impact of the somatic items differs among the questionnaires.

This study included a large and varied sample of cancer patients and a reference group, and, therefore, the results of this study seem generalizable to clinical settings. In further research, these findings must be confirmed in prospective studies.

A limitation of the study was that it applied a cross-sectional design and that no external criterion for depression was used—for instance, a standard psychiatric interview.

In conclusion, the use of questionnaires to assess depression symptoms in the medical setting is valuable because of the high prevalence of depression to be found there. The incidences of somatic morbidity within cancer types differs, but somatic items do not interfere with the outcome of depression as measured with the CES–D. The CES–D seems accurate in measuring depression in cancer patients and appears to be useful in clinical practice.

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APPENDIX 1. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) Criteria for Depression

1. depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others
2. markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
3. significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
4. insomnia or hypersomnia nearly every day
5. psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. fatigue or loss of energy nearly every day
7. feelings of worthlessness or excessive or inappropriate guilt
8. diminished ability to think or concentrate, or indecisiveness, nearly every day
9. recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Furthermore:
The symptoms do not meet criteria for a mixed episode.
The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse; a medication) or a general-medical condition (e.g., hypothyroidism).
The symptoms are not better accounted for by bereavement (i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation).

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